Complete Summary

GUIDELINE TITLE

Metabolic syndrome.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Metabolic syndrome. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2007 Dec 13 [Various].

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Metabolic syndrome. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 Sep 9 [Various].

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 26, 2008, Avandia (rosiglitazone): A new Medication Guide for Avandia must be provided with each prescription that is dispensed due to the U.S. Food and Drug Administration's (FDA's) determination that this medication could pose a serious and significant public health concern.
- November 14, 2007, Avandia (rosiglitazone): New information has been added to the existing boxed warning in Avandia's prescribing information about potential increased risk for heart attacks.
- August 14, 2007, Thiazolidinedione class of antidiabetic drugs: Addition of a boxed warning to the updated label of the entire thiazolidinedione class of antidiabetic drugs to warn of the risks of heart failure.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Metabolic syndrome (MBS)

Conditions that may be associated with MBS, such as

- Type 2 diabetes
- Cardiovascular disease
- Alzheimer's disease

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Endocrinology
Family Practice
Internal Medicine

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients with suspected or known metabolic syndrome (MBS)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Waist circumference
2. Fasting serum triglyceride level
3. Fasting serum high-density lipoprotein cholesterol level
4. Blood pressure
5. Fasting plasma glucose level
6. Oral glucose tolerance test
7. Consideration of other important signs/clinical findings supporting diagnosis including familial component, obesity, abnormal glucose tolerance test result, hyperuricemia, microalbuminuria, hyperinsulinemia

Treatment/Secondary Prevention

Non-pharmacologic

1. Physical activity
2. Weight reduction
3. Change in eating habits
4. Smoking cessation
5. Limiting alcohol consumption

Drug Treatment

1. Low-dose aspirin, unless contraindicated
2. Management of individual components of metabolic syndrome
    - Highly selective beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, alpha 1 receptor blockers, calcium channel blockers, and angiotensin II receptor antagonists for hypertension
    - Statins for dyslipidemia
    - Fibrates for hypertriglyceridemia
    - Metformin or thiazolidine derivatives or insulin for dysglycemia
    - Biguanides, acarbose, and guar gum for type 2 diabetes
    - Orlistat, sibutramine, or endocannabinoid-receptor blockers to lower weight and reduce fat

Management

1. Physician follow-up for patients on drug therapy
2. Practice nurse follow-up for patients not on drug therapy with physician consultation, if applicable

MAJOR OUTCOMES CONSIDERED

Rate of type 2 diabetes, cardiovascular disease, and Alzheimer's disease

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. **Quality of Evidence: High**

Further research is very unlikely to change confidence in the estimate of effect

- Several high-quality studies with consistent results
- In special cases: one large, high-quality multi-centre trial

B. **Quality of Evidence: Moderate**

Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

- One high-quality study
- Several studies with some limitations

C. **Quality of Evidence: Low**

Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

- One or more studies with severe limitations

D. **Quality of Evidence: Very Low**

Any estimate of effect is very uncertain.

- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

The Aim

- Primary and secondary prevention of type 2 diabetes, cardiovascular disease (hypertension, coronary heart disease, stroke, intermittent claudication), and possibly also Alzheimer's disease

Definition of Metabolic Syndrome (MBS)

- MBS is a clustering of risk factors for type 2 diabetes and cardiovascular diseases. The risk factors are associated with obesity, insulin resistance, endothelial dysfunction, and possibly with cellular membrane disruption (Reaven, 1988; Laakso, 1993).
- The clustering of risk factors results in a higher risk of type 2 diabetes and cardiovascular disease than would be estimated if each individual factor were taken into account separately (Tuomilehto et al., 2001; McNeil et al., 2005) Insulin resistance associated with obesity, plays an important role in the accumulation of the components of MBS in any one individual.
- In insulin resistance, the biological response to insulin is impaired in the adipose tissues, muscles, the liver, and possibly the brain. The core abnormality of the syndrome includes the clustering of insulin resistance, compensatory hyperinsulinaemia, and dyslipidaemia in an obese hypertensive.
- MBS is usually evident from truncal obesity which can be detected in clinical practice by measuring the circumference of the waist. MBS is rare in slim individuals (Vanhala et al., 1998).
- The presence of MBS may be detected through medical history, anthropometry, blood pressure readings and by measuring
    - Lipid values
    - Blood or plasma glucose (glucose tolerance test or postprandial glucose if fasting glucose is normal).

The Diagnosis of MBS

- According to the International Diabetes Federation (IDF) consensus 2005, the diagnostic criteria of MBS are:
    1. Central obesity, defined as waist circumference of $\geq$94 cm for Europid men and $\geq$80 cm for Europid women PLUS
    2. At least two of the following factors:
        1. Increased serum triglyceride level: fasting value $\geq$1.70 mmol/L, or specific treatment for this lipid abnormality
        2. Reduced serum high-density lipoprotein (HDL)-cholesterol: fasting concentration <1.03 mmol/L in males and <1.29 mmol/L in females, or specific treatment for this lipid abnormality
        3. Elevated blood pressure(BP): systolic BP $\geq$130 mmHg or diastolic BP $\geq$85 mmHg, or treatment of previously diagnosed hypertension
        4. Increased fasting plasma glucose: $\geq$5.6 mmol/L, or previously diagnosed type 2 diabetes. If the value is above 5.6 mmol/L, oral glucose tolerance test is strongly recommended but is not necessary to define the presence of the syndrome.
- Other important signs and clinical findings supporting the diagnosis include:
    - Familial component: first-degree relative with type 2 diabetes
    - Obesity: body-mass-index (BMI) $\geq$30 kg/m^2. For calculation see programme 1 included in the original guideline document.
    - Abnormal glucose tolerance test result: impaired glucose tolerance (IGT) or type 2 diabetes (NIDDM= non-insulin-dependent diabetes mellitus) according to World Health Organization [WHO] criteria)
    - Hyperuricaemia: fasting serum urate $\geq$450 micromoles/L in men, $\geq$340 micromoles/L in women

    - Microalbuminuria: urine albumin $\geq$20 milligrams/24 hours
    - Hyperinsulinaemia: fasting plasma insulin $\geq$78 pmol/L ($\geq$13.0 mU/L)
- Alzheimer's disease, depression, and sleep apnoea may also be associated with MBS.

Prevalence

- According to the IDF criteria, the prevalence of MBS in a middle-aged population is 38% for men and 34% for women (Alexander et al., 2003).
- About one half of hypertensive patients are hyperinsulinaemic and/or have insulin resistance (Reaven, Lithell, & Landsberg, 1989). In Finnish population, almost half of hypertensive patients fulfill the criteria for MBS (Vanhala et al., 1997).

Treatment

- The treatment is principally non-pharmacological and based on lifestyle changes. This approach has been shown to have an excellent effect, for example in the prevention of diabetes (DPS Study) (Tuomilehto et al., 2001; Knowler et al., 2002) [**A**].
- Lifestyle changes are the only treatment form which have an effect on all the components of MBS, and not employing this treatment should be considered ethically wrong.

Non-Pharmacological Treatment

- Increasing physical activity
- Weight reduction
- Dietary changes: increased intake of fibre and decreased intake of fat (particularly saturated fat) and rapidly metabolised carbohydrates (highly refined); salt restriction
- Cessation of smoking
- Limit alcohol intake to a moderate level

Drug Treatment

- Drug treatment encompassing the entire MBS does not exist, and treatment should therefore consist of the management of the individual components of the syndrome.
- Unless contraindicated, all patients with MBS should be prescribed low dose aspirin.
- The treatment of hypertension in a patient with MBS should not contain drugs that worsen insulin resistance, such as non-selective beta-blockers and high-dose diuretics, unless other reasons (secondary prevention of myocardial infarction) warrant their use. The first-line drugs for the treatment of hypertension are:
    - Angiotensin-converting enzyme (ACE) inhibitors
    - Angiotensin-II receptor antagonists (losartan, valsartan, eprosartan, candesartan)
    - Alpha1 receptor blockers
    - Calcium-channel blockers
    - Highly selective beta-blockers

- Dyslipidaemia in a patient with MBS should principally be treated with statins bearing in mind that the patient has a high risk of coronary artery disease.
- Hypertriglyceridaemia should be treated with fibrates if, in spite of non-pharmacological treatment, the triglyceride values are persistently >5.0 mmol/L. Hypertriglyceridaemia in a patient with MBS should be treated medically (statin or fibrate) if the level of triglycerides is >2.30 mmol/L and total-cholesterol/HDL-cholesterol ratio is higher than 5 or if HDL-cholesterol is lower than 0.9 mmol/L.
- Dysglycaemia in a patient with MBS should be treated with metformin or thiazolidine derivatives (pioglitazone or rosiglitazone) since these will not only improve the dysglycaemia but will also have an effect on the other components of the MBS. Insulin may also be used for the treatment of dysglycaemia in a MBS patient to achieve good diabetic control.
- Biguanides, acarbose, and guar gum may correct insulin resistance and are thus feasible as a first-line drug for an obese patient with type 2 diabetes.
- Orlistat or sibutramine may be indicated in MBS if the BMI is >30 kg/m^2. These are anti-obesity drugs that also reduce the amount of visceral fat, in particular. However, the new endocannabinoid-receptor blockers are likely to provide the best benefit among pharmacotherapeutic alternatives. Rimonabant is an example of these drugs, and it has a positive effect on almost all the components of MBS.
    - Rimonabant should not be prescribed if the patient is concurrently in severe depression. It should be prescribed with caution and the patient should be carefully followed up if he/she has a history of depression.

Follow-up of a Patient with MBS

- Motivation and monitoring of lifestyle changes is of the utmost importance.
- The monitoring of a patient who requires drug treatment is the responsibility of a doctor. Regular appointments may often act as an important motivator.
- The monitoring of a patient who does not require drug treatment may be carried out by a practice nurse. The following should be included in the follow-up: motivation of lifestyle changes, weight and waist circumference measurements, blood pressure readings, and checking of blood lipids and fasting blood glucose. A doctor should be consulted if:
    - Blood pressure repeatedly >140 mmHg and/or >90 mmHg
    - Total cholesterol: HDL-cholesterol ratio >5
    - Triglyceride values repeatedly $\geq$2.30 mmol/L
    - Plasma glucose is $\geq$7.8 mmol/L (fasting plasma glucose is $\geq$6.7 mmol/L
    - The patient develops symptoms of another illness (gout, etc.)

Definitions:

Levels of Evidence

A. **Quality of Evidence: High**

Further research is very unlikely to change confidence in the estimate of effect

- Several high-quality studies with consistent results

- In special cases: one large, high-quality multi-centre trial

B. **Quality of Evidence: Moderate**

Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

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- One or more studies with severe limitations

D. **Quality of Evidence: Very Low**

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- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis and treatment of the metabolic syndrome

- The aim for treating metabolic syndrome (MBS) is for the primary and secondary prevention of type 2 diabetes, cardiovascular disease (hypertension, coronary heart disease, stroke, claudication), and Alzheimer's disease.

POTENTIAL HARMS

If a hypertensive patient has metabolic syndrome, it is important to avoid non-selective beta-blockers and high-dose diuretics, as these drugs may worsen insulin resistance.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jun 29 (revised 2007 Dec 13)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Mauno Vanhala

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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This guideline updates a previous version: Finnish Medical Society Duodecim. Metabolic syndrome. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 Sep 9 [Various].

GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

A body mass index (BMI) calculator is available in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 30, 2005. This summary was updated by ECRI on October 27, 2005. This summary was updated by ECRI on January 11, 2006 following the U.S. Food and Drug Administration advisory on rosiglitazone. This NGC summary was updated by ECRI Institute on January 2, 2008. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration advisory on Avandia (rosiglitazone maleate).

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